Office of Blood Research and Review

Mary Elizabeth Jacobs, Ph.D.
Acting Deputy Director

Our topics....

- Blood Industry
- OBRR Mission
- Who we are
- How is Blood made safe?
- Critical Activities
- Review

Blood Industry

- Blood for transfusion
  - 13.9 million blood units per year collected from 8 million donors at 3,000 registered facilities
  - 18 million components used in 3.5 million recipients per year
  - Major uses in trauma, medical emergencies (e.g. bleeding ulcer), cancer therapy, elective surgery, obstetrics

Blood Industry

- Plasma for further manufacturing
  - 12 million units of Source Plasma per year collected from 1 million donors at 450 licensed facilities , plus 2 million units of plasma “recovered” from whole blood donations
  - 35 different plasma derivative products (e.g. Factor VIII, Factor IX, alpha-1 PI, immune globulins, albumin) used in 500,000 patients/y
  - Major uses in shock, congenital immune deficiency, hemophilia, and infectious disease prevention (e.g. tetanus, HAV)

OBRR Mission

- Regulatory oversight of the safety, efficacy and availability of blood products and retroviral diagnostic tests
- OBRR Functions
  - Establish policies and standards
  - Review applications
  - Conduct lot release
  - Perform establishment inspections and product investigations; assist in compliance actions
  - Make health hazard assessments
  - Carry out mission-related research
  - Counter-terrorism research/policies/implementation

OBRR Priority Initiatives FY‘04

- PDUFA
- MDUFMA
- Counter-terrorism
- Improve Operations
- Globalization of Activities
- Product Safety and Availability
- Outreach
- Mission related research

Office of Blood Research and Review

- **Jay S. Epstein, M.D., Director**
- **Mary Elizabeth Jacobs, Ph.D., Acting Deputy Director**
- **Edward Tabor, Ph.D., Associate Director for Medical Affairs**
- **Linda A. Smallwood, Ph.D., Associate Director for Policy**

OBRR Divisions

- **Division of Blood Applications**
- **Division of Emerging and Transfusion Transmitted Diseases**
- **Division of Hematology**

Division of Blood Applications

- **Director – Alan Williams, Ph.D.**
- **Regulatory Program Management Branch – Sayah Nedjar, Ph.D.**
- **Devices Review Branch – Sheryl Kochman**
- **Blood and Plasma Branch – Elizabeth Callaghan, Acting (also Deputy)**

DBA functions

- RPMs for DETTD and DH
- Manage submissions
- Submission tracking
- Regulatory Policy
- Review:
  - Blood and plasma licenses
  - Blood establishment software
  - Blood grouping reagents

Division of Emerging and Transfusion Transmitted Diseases

- **Hira Nakhasi, Ph.D., Director**
- **Paul Mied, Ph.D., Deputy Director**
- **Indira Hewlett, Ph.D., Director, Laboratory of Molecular Biology**
- **Gerardo Kaplan, Ph.D., Laboratory of Hepatitis and Related Emerging Agents**
- **David Asher, M.D., Laboratory of Bacterial, Parasitic, and Unconventional Agents**

Division of Hematology

- **Basil (Dov) Golding, M.D., Director**
- **Andrew Chang, Ph.D., Acting Deputy Director**
- **Jaro Vostal, M.D., Ph.D., Chief, Laboratory of Cellular Hemostasis**
- **Dorothy Scott, M.D., Chief, Laboratory of Cellular Hematology**
- **Andrew Chang, Ph.D., Acting Chief, Laboratory of Hemostasis**
- **Toby Silverman, M.D., Chief, Clinical Review Branch**

How to contact OBRR about your submission/issues

- **Website – many reference materials**
- **Set up a meeting – Nedjar/Kochman**
- **Resolve issues**
  - **Go through RPM first**
  - **Set up conference call with reviewers/SL**
  - **Contact Division management**
  - **Contact Office – Mary Beth Jacobs**

Outside Interactions

- **Blood Products Advisory Committee**
  - **Scientific Advisory Committee**
  - **Transcripts and Documents on Web**
- **Advisory Committee on Blood Safety and Availability**
  - **Reports to Assistant Secretary for Health, DHHS**
  - **Can consider cost**
- **PHS Blood monthly conference call**
  - **All PHS agencies (FDA, CDC, NIH) and DOD**
- **Stakeholder meetings**

How Is Blood Made Safe?

- Five Layers of Blood Safety
  - **Selection of suitable donors**
    - **Donor education and risk factor screening**
    - **Medical interview**
    - **Limited physical examination**
  - **Use of deferral registries to identify unsuitable donations**
  - **Infectious disease testing (HIV, HCV, HBV, HTLV, STS, CMV,WNV)**
  - **Quarantining blood while verifying suitability and doing tests**
  - **Monitoring, investigating and taking corrective actions to address errors, accidents, and adverse reactions**

How Is Blood Made Safe? *(cont.)*

- Product standards
  - **e.g. sterile collection, closed systems, viral inactivation**
  - **Research based**
- Current Good Manufacturing Practices
  - **Process validation,**
  - **Labeling controls,**
  - **Quality control testing,**
  - **Employee training/certification,**
  - **Audits.**

Example: West Nile Virus

- Sept. 4, 2002: CDC notifies CBER that WNV can be transmitted by blood and cause illness
- November, 2002: FDA Workshop with stakeholders
- Updates at BPAC
- Very active interaction and problem solving with regulated industry

Example: WNV (cont.)

- Research in OBRR labs to develop lot release panel
- Sensitivity of assay set
- INDs approved
- June 2003: first testing of donations begins
- By July 1, 2003 100% of military, 95% civilian donations screened
- 1000+ positive WNV donations identified

Blood Action Plan - Current Initiatives

- **Rulemaking:**
  - **HCV Lookback (Final Rule and Guidance)**
  - **Uniform Labeling**
  - **Donor Eligibility Requirements**
  - **Infectious Agent Clearance**
- **Guidance:**
  - **Biological Product Deviation**
  - **NAT Implementation Guidance**
- **Monitoring blood supply and demand**

Approach to Medical Errors

- Approval of new technologies that reduce error
  - **Automation; software; standard labeling; patient ID's**
- Required reporting of fatalities and product deviations
- Further rulemaking (standard labeling; reporting of serious adverse events)
- Development of a Medical Event Reporting System for Transfusion Medicine (MERS-TM)
- Barcoding rule

Areas of Mission-Related Research

- Safety, efficacy and standardization of clotting factors and immune globulin products
- New virus detection methods (e.g. NAT)
- Toxicity of oxygen-carrying compounds
- TSE detection, pathogenesis and removal
- Structure/function of wbc's and platelets
- Epidemiology of viral variants (HIV, HBV)
- Diagnostic tests for parasitic diseases

Counter Terrorism Research

- CT now 25% of CBER effort/resource use
- Proactive needs/gap assessments/inventories
- Participate in multiple Task Forces
- Implementation of Project Bioshield
- Diagnostic and pathogenic investigations of smallpox and its implications for blood safety
- Detection of Bioterror Pathogen Nucleic Acid in Blood Using Novel Technologies
- TRANS-NET, a web-based electronic system for voluntary reporting of blood, blood products, reagents and supply shortages to the FDA by U.S. blood centers and transfusion services.

Counter Terrorism Research 2

- **Selecting an immunogen/vaccine for production of high-titer anti-anthrax immune globulin in sheep**
- **Measurement of the potency of Vaccinia Immune Globulins**
- **Vaccinia Immune Globulin: Efficacy and Mechanism of Action in Vaccinia- infected Murine Models with various Immune Dysfunctions.**
- **Characterization of Anti-Vaccinia Antibodies in Licensed Immune Globulins (Intravenous, human)**

Products Evaluated

- Blood and plasma components
- Plasma derivatives
- Donor screening tests
- Blood grouping reagents
- Devices used in blood collection, storage and processing
- Blood bank and related computer software
- HIV tests

Commitment to Managed Review

- Disciplined Approach
- Regulatory Project Manager
- Management Structure/responsibilities
- Training
- Adhere to policies
- Electronic Submissions and secure email

PDUFA Issues

- User fees support over 30% of CBER operations;
- Now in PDUFA 3
- Reviews of blood components and devices are not supported by user fees
- OBRR must expend “base” resources to meet PDUFA requirements, shortchanging the non-user fee program
- New Guidances

MDUFMA

- Oversight of Combination Product Review
  - RFD
- Fees for Application Review
- Reports to Congress on meeting review performance goals
- Review performance now comparable to CDRH

Review Workload-FY 2003

- IND/IDE/MF's Received: original 93, amendments 1263
- Product Reviews Completed: 1116
  - BLA's: original 20, supplements 934
  - PMA's: original 2, modular 3, suppl.'s 22, modules 20
  - NDA's: original 3, supplements 44
  - ANDA's: original 1, supplements 3
  - 510(k)'s: 64

CBER Device Application Receipts

FY 2002 – FY 2004*

		MDUFMA	
	FY02	FY03	FY04*
PMAs (Traditional)	0	0	0
PMAs (Modular)	1	3	0
PMSs (180 Day)	5	3	2
510(k)s (All Types)	40	65	24
BLAs (Original)	2	0	1
BLSs (Efficacy)	0	3	0
BLSs (Manuf, PAS)	35	75	5

* FY 04 numbers for first four months - as of January 31, 2004

CBER 510k Review Time Performance
Receipt to Final Action
FY 2002-FY2004*

MDUFMA

	FY02	FY03	FY04*
CBER Review Time (days)	119.1	57.6	58.7
Average Number of Cycles	1.7	1.3	1.1

Includes SEs/NSEs/WDs

*FY 04 data for first four months through January 31, 2004

Please let us know

- Your concerns
- Your questions
- Thanks for your attention